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DATA EVALUATION REPORT

ZIRAM

STUDY TYPE: DERMAL SENSITIZATION - GUINEA PIG (81-6)

8/2/2000

Prepared for

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Prepared by

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ZIRAM Dermal Sensitization Study (OPP 81-6; OPPTS 870.2600)

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DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea Pig
OPPTS 870.2600 [§81-6]

DP BARCODE: D235025
P.C. CODE: 034805

SUBMISSION CODE: S521512
TOX. CHEM. NO.: 931

TEST MATERIAL (PURITY): Ziram Technical (99.04%)

SYNONYMS: Zinc dimethyldithiocarbamate

CITATION: Daamen, P.(1988) Assessment of the skin sensitization potential of Ziram Technical in the guinea-pig (Split Adjuvant Test). RCC NOTOX C.V., Hambakenwetering 7, 5231 DD s-Hertogenbosch, The Netherlands. Laboratory project identification RCC NOTOX 0878/1096, June 9, 1988. MRID 41643003. Unpublished.

SPONSOR: UCB S.A., 326, Avenue Louise, B-1050 Brussels, Belgium

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 41643003) with Ziram Technical (99.04% a.i., Batch no. 8331AA) in corn oil, 20 young adult female Dunkin-Hartley guinea pigs were tested using the Split Adjuvant Technique and 10 animals were used as controls. For the induction phase, the Ziram technical (25% w/w in corn oil) was applied dermally on days 1, 2 and 7; Freund's complete adjuvant was injected intradermally to treated and control animals on day 4. For the challenge phase, each test animal had 24-hour dermal applications of the test material in corn oil (0, 1, 5 and 10% w/w). Twenty-four and 48 hours after the challenge, the treated sites were scored for erythema and edema.

In the induction phase, no dermal reaction data were presented. In the primary dermal irritation study (conducted to determine the challenge phase concentrations), all concentrations (5-50%) showed slight dermal irritation.

In the challenge phase, 24 hours after the challenge dose, 6/20 (10% concentration), 5/20 (5% concentration), 2/10 (1% concentration) showed a dermal reaction (grade 2 or 3). At 48 hours, some animals still had signs of a dermal reaction. Therefore, under the conditions of this study, **Ziram Technical is a moderate dermal sensitizer, based on a 30% sensitization rate.**

This study is classified as acceptable (guideline) and satisfies the guideline requirement for a dermal sensitization study (81-6) in the guinea pig.

The positive control study was not done within approximately 6 months of the definitive study, as suggested by the test guidelines. However, this should not affect the validity of the study results.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ziram Technical

Description: greyish-white solid
Lot/Batch #: 8331AA
Purity: 99.04% a.i.
CAS #: 137-30-4

2. Vehicle and positive control

Vehicle - corn oil; positive control (in separate study) - induction: 5% w/w formaldehyde in distilled water, challenge: 0.5, 2, and 5% formaldehyde in distilled water

3. Test animals

Species: female guinea pig
Strain: Dunkin Hartley
Age and weight at start of treatment: ~2 months; 287-413 g (3-6 days before dosing)
Source: Charles River Wiga, FRG
Acclimation period: 13 days
Diet: ascorbic acid (1600 mg/kg) fortified standard guinea pig diet (LC 23-B, pellet diameter 4 mm), *ad libitum*, hay was also provided once/week
Water: drinking water, *ad libitum*
Housing: 2/metal cage with wire-mesh floor
Environmental conditions:
Temperature: 19-25°C
Humidity: 60-85%
Air changes: not reported
Photoperiod: 12 hour light/dark

B. STUDY DESIGN AND METHODS

1. In life dates

Definitive study - Start: May 10, 1988 (primary irritation experiment); end: June 9, 1988 (Split Adjuvant Test)
Positive control study - February 1987

2. Animal assignment and treatment

A primary irritation test was carried out using 5 animals to determine the concentration to be applied in the challenge phase. Four animals were exposed to 0.05 ml of 50%, 25%, 10% and 5% (w/w) of the test substance in corn oil on their flanks for 24 hours. An additional animal received 0.5 ml of 50% of the test substance in corn oil for 24 hours to evaluate the toxicity of the material. Severe erythema was observed in one animal at the 25% and 10% treatment sites. Other animals had very slight or no erythema. No systemic toxicity was observed in any of the animals.

In the definitive study, the test animals were induced and challenged according to the Split Adjuvant Technique.

Induction Phase: An area on the back just behind the right shoulder girdle of 30 female guinea pigs was shaved. Each animal was wrapped in a ▒window dressing▒ which consisted of Coban elastic bandage. A 2 x 2 cm opening was cut in the dressing over the exposure site. Dry ice was applied to the test site for ~5 seconds. To 20 guinea pigs, 0.2 mL of test material (25% w/w in corn oil) was applied and covered with a Metalline-patch, then covered with water-impervious tape. On day 2, the dressing that covered the window was removed, 0.2 mL of test material in corn oil was applied, and the window was reclosed with the same dressing. On day 4, the window was again opened and 0.1 mL of Freund's complete adjuvant was injected intradermally on both sides of the exposure site. This was followed by a further dermal application of 0.2 mL of the test material in corn oil, and the window was closed. On day 7, the test material was again applied. On day 9, all wrappings were removed. On day 4, the 10 negative control animals received intradermal injections of Freund's complete adjuvant.

Challenge Phase: On day 21, the flanks of all animals were shaved. The test material in corn oil was applied at a volume of 0.05 mL on Square Chambers, mounted on Micropore-tape. Each animal received 4 different concentrations (0, 1, 5, and 10% w/w in corn oil) of test material; all animals were treated similarly. The Coban elastic bandage was kept in place for 24 hours. Twenty-four and 48 hours after patch removal the challenge site was scored for erythema and edema.

Positive Control: Approximately 15 months earlier, a positive control study was done by the laboratory. The basic technique was not described but presumably was identical to the above procedure with the exception that the induction phase was 5% w/w formaldehyde solution (37%) in Milli-RO water, and challenge phase was 0.5, 2, and 5% w/w formaldehyde in Milli-RO water.

II. RESULTS AND DISCUSSION

A. INDUCTION REACTIONS

Dermal reactions during the induction period were not reported. The primary dermal irritation part of the study showed that all animals

which received the test material at various concentrations (5-50%) had slight dermal irritation.

B. CHALLENGE REACTIONS AND DURATION

Twenty-four hours after challenge, positive skin responses (moderate but confluent redness or redness and swelling, grade 2 or 3) were noted in reaction to the 10% challenge concentration in 6 animals, the 5% concentration in 5 animals, and the 1% concentration in 3 animals. Eight animals showed red spots in reaction to one or more of the challenge concentrations. At 48 hours,the following number of animals still had scores of 2 or 3: 3 at 10%; 3 at 5%; and 2 at 1%. No skin reactions were observed in the negative control animals, with the exception of one animal that showed red spots in reaction to the 5 and 10% test material concentration. Based on these results, a sensitization rate of 30% was obtained. Ziram Technical is a moderate sensitizer to the skin of female Hartley guinea pigs.

C. POSITIVE CONTROL

A sensitization rate of 50% was obtained to the 0.5% w/w formaldehyde solution.

D. DEFICIENCIES

The postive control study was done approximately 15 months before the definitive study. Guidelines suggest the periodic use of a positive control (approximately every 6 months). However, since positive results were obtained, this should not affect the validity of the study results.

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